-continued

Pro	Lys	Asp	Thr 20	Leu	Met	Ile	Ser	Arg 25	Thr	Pro	Glu	Val	Thr 30	Cys	Val					
Val	Val	Asp 35	Val	Ser	His	Glu	Asp 40	Pro	Glu	Val	Lys	Phe 45	Asn	Trp	Tyr					
Val	Asp 50	Gly	Val	Glu	Val	His 55	Asn	Ala	Lys	Thr	Lys 60	Pro	Arg	Glu	Glu					
Gln 65	Tyr	Asn	Ser	Thr	Tyr 70	Arg	Val	Val	Ser	Val 75	Leu	Thr	Val	Leu	His 80					
Gln	Asp	Trp	Leu	Asn 85	Gly	Lys	Glu	Tyr	Lys	Суз	Lys	Val	Ser	Asn 95	Lys					
Ala	Leu	Pro	Ala 100	Pro	Ile	Glu	Lys	Thr 105	Ile	Ser	Lys	Ala	Lys 110	Gly	Gln					
Pro	Arg	Glu 115	Pro	Gln	Val	Tyr	Thr 120	Leu	Pro	Pro	Ser	Arg 125	Asp	Glu	Leu					
Thr	Lys 130	Asn	Gln	Val	Ser	Leu 135	Thr	Cha	Leu	Val	Lys 140	Gly	Phe	Tyr	Pro					
Ser 145	Asp	Ile	Ala	Val	Glu 150	Trp	Glu	Ser	Asn	Gly 155	Gln	Pro	Glu	Asn	Asn 160					
Tyr	Lys	Thr	Thr	Pro 165	Pro	Val	Leu	Asp	Ser 170	Asp	Gly	Ser	Phe	Phe 175	Leu					
Tyr	Ser	ГÀв	Leu 180	Thr	Val	Asp	Lys	Ser 185	Arg	Trp	Gln	Gln	Gly 190	Asn	Val					
Phe	Ser	Cys 195	Ser	Val	Met	His	Glu 200	Ala	Leu	His	Asn	His 205	Tyr	Thr	Gln					
ГÀа	Ser 210	Leu	Ser	Leu	Ser	Pro 215	Gly	ГÀв												

We claim:

- 1. A method of treating a subject having a tumor; inhibiting, reducing or blocking HER2 signaling; or killing or inhibiting the growth of a HER2-expressing tumor cell, the method comprising administering an effective amount of an antigen binding construct comprising:
 - a first antigen-binding polypeptide construct which monovalently and specifically binds a HER2 (human epidermal growth factor receptor 2) ECD2 (extracellular domain 2) antigen on a HER2-expressing cell;
 - a second antigen-binding polypeptide construct which monovalently and specifically binds a HER2 ECD4 (extracellular domain 4) antigen on a HER2-expressing cell:
 - first and second linker polypeptides, wherein the first linker polypeptide is operably linked to the first antigen-binding polypeptide construct, and the second linker polypeptide is operably linked to the second antigen-binding polypeptide construct;
 - wherein the linker polypeptides are capable of forming a covalent linkage with each other,
 - wherein one or both of the first or the second antigen binding polypeptide construct is an scFv, and optionally wherein the antigen binding construct is conjugated to DM1,
 - wherein the dissociation constant (K_D) of the antigen binding construct to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR) is equal to or less than the dissociation constant

- of a monospecific anti-HER2 ECD4 antibody (v506; SEQ ID NO:1 and SEQ ID NO:317) to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR), and
- wherein tumor growth is decreased as compared to a control receiving an equivalent amount of a non-specific control antibody, as compared to a control receiving an equivalent amount of Herceptin/trastuzumab, or as compared to a control not receiving treatment.
- 2. The method of claim 1 wherein the antigen binding construct comprises the full length sequences set forth in SEQ ID NOs 97, 295, and 69 (v10000), and optionally wherein the dissociation constant (K_D) of the construct to murine HER2 extracellular domain as measured by surface plasmon resonance (SPR) is approximately 0.6 nM.
- 3. A method of treating a subject having a tumor; inhibiting, reducing or blocking HER2 signaling; or killing or inhibiting the growth of a HER2-expressing tumor cell, the method comprising administering an effective amount of an antigen binding construct comprising:
 - a first antigen-binding polypeptide construct which monovalently and specifically binds a HER2 (human epidermal growth factor receptor 2) ECD2 (extracellular domain 2) antigen on a HER2-expressing cell, wherein the first antigen-binding polypeptide construct comprises a first variable light-chain (VL1) domain and a first variable heavy-chain (VH1) domain, wherein the first antigen-binding polypeptide construct comprises VH1 and VL1 CDR sequences that are at least 90, 91,